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### **REMARKS**

In the claim listing above, no claims have been amended, added or canceled. Accordingly, claims 251-287 and 625 continue to be presented for further examination in this application.

### **Request For Continued Examination**

Applicants appreciate the acknowledgement in the Office Communication (page 2) that their Request For Continued Examination has been entered and that claims 251-287 and 625 are currently pending.

### **Priority**

The Examiner's comments on pages 2-3 of the Office Communication regarding the priority date for this application are acknowledged. Applicants understand that the instant October 24, 2003 filing date has been used for prior art purposes.

### **Information Disclosure Statement**

According to the Office Communication (page 3):

The information disclosure statement filed on September 18, 2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Specifically, references 20-25, 42-47, 50, and 51 have not been considered, because a copy of these foreign patent documents or non-patent literature publications has not been provided.

In response, Applicants note that they have already submitted the ten documents referenced above in their June 19, 2009 Information Disclosure Statement that was filed by Express Mail. Also submitted in their June 19, 2009 IDS were nine

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additional documents. All nineteen documents were listed on four IDS forms, also submitted.

#### **Withdrawal of Previous Rejections**

Applicants appreciate the indication in the Office Communication (page 18, item 11) that in view of amendments in their last paper the previous objections to the specification and the claims have been withdrawn.

There are seven obviousness rejections that were made in the December 22, 2008 Office Communication.

#### **Commonality of Ownership**

Applicants assert that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made.

#### **The First Rejection Under 35 USC §103**

Claims 251-264, 269-273, 275, 281-286, and 625 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1 201768 A2; cited previously). Comments directed to the first rejection are set forth on pages 4-9 in the Office Communication.

The first obviousness rejection is respectfully traversed.

With regard to this particular combination of the Lin and Laird documents, Applicants respectfully point out that the latter is wholly concerned with the elimination of non-specific priming by the use of modified nucleotides at the terminal ends of primers. Indeed, in Column 1, lines 53-67, Laird et al. disclose two sources of "non-specific amplification", the first is from nucleic acids in a sample that were not the target of the amplification:

Under less stringent conditions, the primers may bind non-specifically to other only partially complementary nucleic acid sequences or to other

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primers and initiate the synthesis of undesired extension products, which can be amplified along with the target sequence." (Column 1, lines 53-67)

Laird et al. then go on to note in the next column:

One frequently observed type of non-specific amplification product is a template independent artifact of amplification reactions referred to as primer-dimer. Primer/dimer is a double-stranded fragment whose length typically is close to the sum of the two primer lengths and appear to occur when one primer is extended over the other primer.[Column 2, lines 5-10]

Applicants respectfully note, however, that such as disclosed by Laird et al. is actually not "template independent" because a primer is actually used as a template. Rather, the product disclosed by Laird et al. is a target-template independent artifact.

Furthermore, in the absence of the present disclosure, no particular advantage would be seen by combining the disclosures of Laird et al. and Lin et al. First, because theirs is a linear amplification system rather than an exponential system like PCR, Lin et al. do have a problem with primer-dimer synthesis. Secondly, it would not be expected that the primers used by Lin would have ever have problems with primer/dimer artifacts even if they were used in a PCR reaction, since as noted by Laird, the consensus explanation for the production of these amplimers is partial homology of sequences at the 3' end of primers allow mis-priming events where one primer is used as a template by another primer. As such, one would have to have some variety in the 3' end sequences rather than the homopolymers used by Lin as well as practiced in the present invention. That is to say, there is no partial homology (and consequently, no base-pairing) between two poly T primers.

Thirdly, the major point of the Laird's disclosed method is for discrimination between target and non-target nucleic acid templates. This was discussed in Applicants' previous response as well as the specification itself, where the Laird 6,794,142 patent was discussed in the context of the its published application, 2003/0044817 (See column 5, [0043] of the published version of this disclosure 2006/0057583). The point made here is rather than a requirement of a discrete synthesis of a particular nucleic acid sequence as is usually carried out by PCR, the library amplification carried in the

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present invention as well as by Lin et al., is for the amplification of any and all poly A sequences regardless of their sequence. As such there is no relevancy to a potential increase in discrimination between target and non-target nucleic acid templates, as all sequences are considered to be targets in a global amplification system. In contrast, Laird et al. is mostly concerned with PCR and then noted other systems that could use this system (as noted in the Office Action) where all references were to other analyte specific amplification systems where the discrete amplification over other non-target nucleic acids was advantageous. No global amplification systems are listed in this group.

Applicants respectfully disagree with the statement made in the Office Communication (page 8) that the use of Laird et al. in conjunction with the teachings of Lin would have reasonable expectations of success, when "success" is defined by criteria that are irrelevant to Lin. Applicants are unable to define which non-specific amplification is hoped to be cured by the application of Laird to the teachings of Lin.

On the other hand, the present invention has made note in the first instance that the presence of terminally modified nucleotides can provide a benefit in that if unextended primers are left over from the first cDNA copying reaction, the presence of these moieties on the primers does not allow the extension by TdT even though reverse transcriptase is able to extend them. Secondly, the inventors have made an unexpected discovery that the use of the modified terminal primers can universally increase the yields of nucleic acid products. Again, this is a universal quality where no distinction is being made for higher efficiency of target nucleic acids at the expense of decreased efficiency of non-target nucleic acids.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the first obviousness rejection.

#### **The Second Rejection Under 35 USC §103**

Claims 265-268 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1201768;

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cited previously) and in further in view of Willis et al. (US 6,858,412; cited previously) and further in view of Moran et al. (Nucleic Acids Research (1996) 24(11): 2044-2052; cited previously). The second rejection is provided on pages 9-11 in the Office Communication.

The second obviousness rejection is respectfully traversed.

In response, Applicants incorporate their remarks from the first obviousness rejection. Because the primary and secondary documents are unable to reach the present invention and claims, then as a matter of logic the addition of yet third and fourth documents in the form of Willis et al. and Moran et al., respectively, must also fail to reach the same invention and claims.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the second obviousness rejection.

#### **The Third Rejection Under 35 USC §103**

Claims 274 and 276 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1201768; cited previously) and further in view of Sousa et al. (US 5,849,546; cited previously). The third rejection is provided on pages 11-13 in the Office Communication.

The third obviousness rejection is respectfully traversed.

Applicants incorporate their remarks from the first obviousness rejection. Because the primary and secondary documents are unable to reach the present invention and claims, then as a matter of logic the addition of yet a third document in the form of Sousa et al. must also fail to reach the same invention and claims.

In light of the foregoing, Applicants respectfully request reconsideration and withdrawal of the third obviousness rejection.

#### **The Fourth Rejection Under 35 USC §103**

Claims 277, 278, and 280 stand rejected under 35 U.S.C. §103(a) as being

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unpatentable over Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1201768; cited previously) and further in view of Steffens et al. (Genome Research (1995)5:393-399; cited previously). The fourth rejection is set forth on pages 13-14 in the Office Communication.

The fourth obviousness rejection is respectfully traversed.

Applicants incorporate their remarks from the first obviousness rejection. Because the primary and secondary documents are unable to reach the present invention and claims, then as a matter of logic the addition of yet a third document in the form of Steffens et al. must also fail to reach the same invention and claims.

Reconsideration and withdrawal of the fourth obviousness rejection is respectfully requested.

#### **The Fifth Rejection Under 35 USC §103**

Claim 279 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1201768; cited previously) and further in view of Sousa et al. (US 5,849,546; cited previously) and further in view of Steffens et al. (Genome Research (1995) 5: 393-399; cited previously). The fifth rejection is set forth on pages 15-16 in the Office Communication.

The fifth obviousness rejection is respectfully traversed.

Applicants incorporate their remarks from the first obviousness rejection. Because the primary and secondary documents are unable to reach the present invention and claims, then as a matter of logic the addition of yet third and fourth documents in the form of Sousa et al. and Steffens et al., respectively, must also fail to reach the same invention and claims.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the fifth obviousness rejection.

#### **The Sixth Rejection Under 35 USC §103**

Claim 287 stands rejected under 35 U.S.C. §103(a) as being unpatentable over

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Lin et al. (US 6,197,554 B1; cited previously) in view of Laird et al. (EP 1201768; cited previously) and further in view of Borson et al. (PCR Methods and Applications (1992) 2: 144-148; cited previously). The sixth rejection is set forth on pages 16-17 in the Office Communication.

The sixth obviousness rejection is respectfully traversed.

Applicants incorporate their remarks from the first obviousness rejection. Because the primary and secondary documents are unable to reach the present invention and claims, then as a matter of logic the addition of yet a third document in the form of Borson et al. must also fail to reach the same invention and claims.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the sixth obviousness rejection.

#### **The Seventh Rejection Under 35 USC §103**

Claim 625 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Borson et al. (PCR Methods and Applications (1992) 2: 144-148; cited previously) in view of Laird et al. (EP 1201768; cited previously). The seventh rejection is set forth on pages 17-19 in the Office Communication.

The seventh obviousness rejection is respectfully

In response, Applicants respectfully point out that the deficiencies in Laird's disclosure are ample and have been noted above in the first obviousness rejection. Those deficiencies in Laird et al. will not support a rejection of claim 625 based upon Borson et al..

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the seventh obviousness rejection.

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### **SUMMARY AND CONCLUSIONS**

A complete listing of the claims in this application are provided above. In the claim listing above, no claims have been amended, added or canceled by this paper.

Applicants' Request For Extension Of Time (3 Months) was previously submitted with their June 19, 2009 Information Disclosure Statement. No other fee or fees are believed due in connection with this paper. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Early and favorable action is respectfully requested.

Respectfully submitted,



Ronald C. Fedus  
Registration No. 32,567  
Attorney for Applicants

ENZO LIFE SCIENCES, INC.  
c/o Enzo Biochem, Inc.  
527 Madison Avenue (9<sup>th</sup> Fl.)  
New York, New York 10022  
Telephone (212) 583-0100  
Fax (212) 583-0116

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